LECTURE 12. FURTHER APPLICATIONS OF THE CANONICAL FORMALISM.

• The Canonical Partition Function as a Sum Over Levels

In the example of the 2-state system with 3 particles, the evaluation of the canonical partition function Q was based on the exhaustive enumeration of all the possible microstates of the system (of which there were 8.) But the problem could also have been approached by first enumerating the possible energy *levels* or energy *macrostates* of the system (of which there were four: 0, ε, 2ε and 3ε), constructing the corresponding Boltzmann weights (1, $e^{-\beta\varepsilon}$, $e^{-2\beta\varepsilon}$ and $e^{-3\beta\varepsilon}$), multiplying these weights by the corresponding *multiplicities* (1, 3, 3 and 1), and then adding up all the results. This leads to the same equation that we arrived at by the original method. In general, then, it's possible to write

$$\sum_{\alpha} e^{-\beta U_{\alpha}(V,N)} = \sum_{U} \Omega(U,V,N) e^{-\beta U} \qquad (1)$$

where $\Omega(U,V,N)$ is the multiplicity of the macrostate of energy U (at some V and N), (and is therefore also the microcanical partition function of the system with those particular thermodynamic variables.) This is an important equivalence that you need to recognize and understand; an illustration of its application is given in the next section.

• Biological Applications: Ligand-Receptor Interactions

Much of what happens inside a living cell is often the end result of processes involving the binding of one or more ligands to a receptor, as illustrated in Fig. 1, which is a sketch of the sequence of steps, starting with ligand-receptor binding, that leads ultimately to changes in the nucleus.

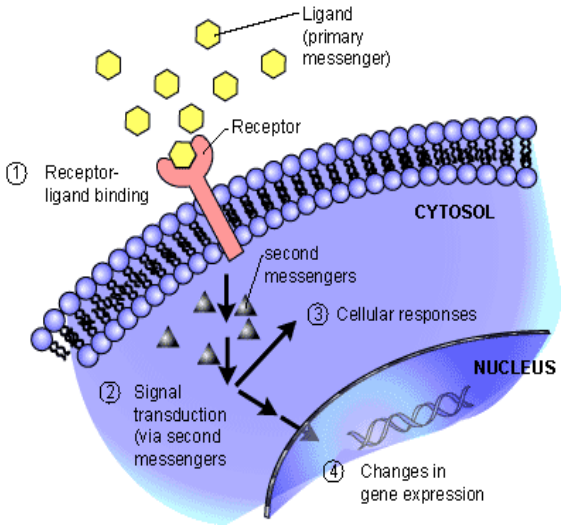


Fig. 1

Cellular receptors like the one above are usually located on the surface of a membrane, and they tend to have very little freedom to move around. Ligands, on the other hand, being located in the extra-cellular medium, are mobile, and travel randomly from one place to another under the action of thermal forces (i.e, solvent fluctuations), binding to a receptor whenever the two are close enough for their mutual attractive interactions to come into play. How often this event takes place will determine the extent to which other downstream events are activated. The frequency of ligand-receptor binding in turn is a function of ligand concentration, and it is clearly probabilistic in nature. A question that then comes to mind is this: given some concentration of ligands and a single receptor to which the ligands can bind, what is the likelihood that binding will in fact occur?

The question has actually been addressed experimentally, in a study of the binding of increasing amounts of oxygen to a fixed concentration of myoglobin (*Arch. Biochem. Biophys*. **77**, 478 (1958).) The results of the study are shown in Fig. 2. The *y*-axis in this figure corresponds to the fraction of myoglobin molecules that are bound to O_2, which can be interpreted as the probability that any *one* myoglobin molecule is O_2-bound. The *x*-axis corresponds to the O_2 partial pressure, which is a measure of how many ligands (O_2) there are.

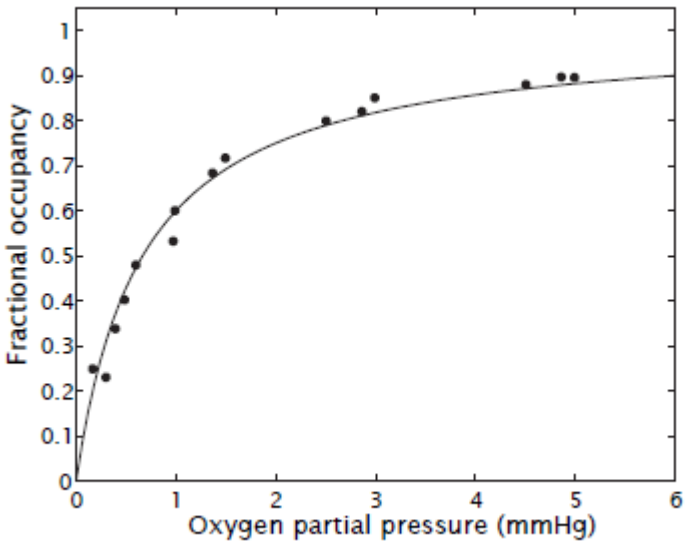


Fig. 2

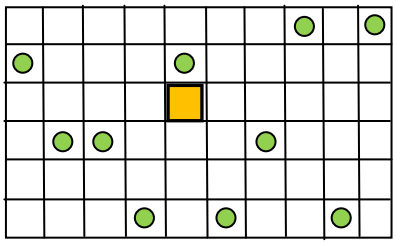
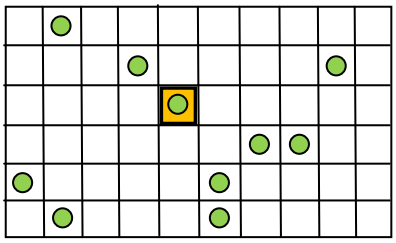
Can data like this be rationalized from a statistical mechanical perspective? We'll now try to answer this question.

• A Microscopic Model of Ligand-Receptor Binding

Let's think of the surface of a membrane on which a receptor is located as a grid composed of N *distinguishable* cells (as in the figures below), with $N >> 1$. We'll assume that a single receptor (yellow square) occupies one of these cells, and that a set of $L << N$ *indistinguishable* ligands (green circles) can occupy any of the others (including the cell with receptor), but without multiple occupancy. We'll also assume that when it is in an empty cell, a ligand has an energy ε_s, and when bound to the receptor, it has an energy ε_b. The entire system is imagined to be in equilibrium at temperature T (through contact with a thermal reservoir), so the ligands are free to move from one cell to the other. A snapshot of the system at some arbitrary time t would be typified by either of the two drawings in the first column of the table, each of which, in effect, represents a *microstate* of the system.

Given this model, what is the probability that a ligand is bound to the receptor?

For a system at constant T, statistical mechanics tells us that the probability of it being in some microstate α is given by $e^{-\beta U_\alpha}/Q$. In the present model, there are two kinds of energy states (i.e. *macrostates*), one in which *no* ligand is bound to the receptor, and the other in which one ligand is. Each of these macrostates has a multiplicity associated with it, which is the number of ways of arranging L ligands amongst the N cells. The energies of the two macrostates are listed in the second column of the table below, and their multiplicities in the third column. As just mentioned, the first column depicts a possible *microstate* of the given macrostate.

State	Energy	Multiplicity
	$L\varepsilon_s$	$\dfrac{(N-1)!}{L!(N-1-L)!} \approx \dfrac{N!}{L!(N-L)!}$
	$(L-1)\varepsilon_s + \varepsilon_b$	$\dfrac{(N-1)!}{(L-1)!(N-L)!} \approx \dfrac{N!}{(L-1)!(N-L+1)!}$

With the information in the table in hand, we can use the *energy levels* representation of the canonical formalism to express the probability that a ligand is bound to the receptor as

$$p_b = \frac{\frac{N!}{(L-1)!(N-L+1)!}\exp\left(-\beta\varepsilon_b - \beta(L-1)\varepsilon_s\right)}{\frac{N!}{L!(N-L)!}\exp\left(-\beta L\varepsilon_s\right) + \frac{N!}{(L-1)!(N-L+1)!}\exp\left(-\beta\varepsilon_b - \beta(L-1)\varepsilon_s\right)} \tag{2}$$

Equation (2) can be simplified by noting that, in general, for some $M >> K$

$$\frac{M!}{(M-K)!} \approx M^K \tag{3}$$

To see why this is a reasonable approximation, consider the case $M = 10^4$ and $K = 10$. Then,

$$\frac{10^4!}{(10^4-10)!} = \frac{10^4 \times (10^4-1) \times (10^4-2) \times \cdots \times 3 \times 2 \times 1}{(10^4-10)!}$$

$$= \frac{10^4 \times (10^4-1) \times (10^4-2) \times \cdots \times (10^4-9) \times (10^4-10)!}{(10^4-10)!}$$

$$= 10^4 \times (10^4-1) \times (10^4-2) \times \cdots \times (10^4-9)$$

$$\approx \left(10^4\right)^{10}$$

Using Eq. (3) in Eq. (2),

$$p_b = \frac{\frac{N^{L-1}}{(L-1)!}\exp\left(-\beta\varepsilon_b - \beta(L-1)\varepsilon_s\right)}{\frac{N^L}{L!}\exp\left(-\beta L\varepsilon_s\right) + \frac{N^{L-1}}{(L-1)!}\exp\left(-\beta\varepsilon_b - \beta(L-1)\varepsilon_s\right)} \tag{4}$$

If a factor of $\frac{N^L}{L!}\exp\left(-\beta L\varepsilon_s\right)$ is pulled out from the denominator, Eq. (4) becomes

$$p_b = \frac{(L/N)e^{-\beta\Delta\varepsilon}}{1+(L/N)e^{-\beta\Delta\varepsilon}} \tag{5}$$

where $\Delta\varepsilon \equiv \varepsilon_b - \varepsilon_s$. If we think of the receptor-model system as having some overall volume *V*, then *L*/*V* can be thought of as a ligand concentration *c*, while *N*/*V* can be thought of as a reference concentration c_0. In terms of these concentrations, Eq. (5) assumes the form

$$p_b = \frac{(c/c_0)e^{-\beta\Delta\varepsilon}}{1+(c/c_0)e^{-\beta\Delta\varepsilon}} \tag{6}$$

For values $\beta\Delta\varepsilon$ on the order of 10 or so, with c_0 chosen to be about 0.6M, a plot of p_b vs. *c* yields a curve that is in highly satisfactory qualitative agreement with data on oxygen binding in Fig. 2 (!)

• <u>The Ideal Gas Revisited</u>

Although this system has already been treated in the microcanonical formalism, we'll study it again in the canonical formalism to highlight an important fact about partition functions: that it doesn't really matter which partition function is used in the calculation of thermodynamic properties; they all lead to essentially the same results. The ideal gas provides a concrete illustration of this fact.

As before, we regard the ideal gas as a collection of *N* independent indistinguishable point particles confined to a box of volume *V*. Each particle exists in one of a number of different quantum mechanical energy states defined by

$$\varepsilon_{jkl} = \frac{h^2}{8mL^2}(j^2+k^2+l^2), \quad j,k,l = 1,2,3,\ldots \tag{7}$$

In some microstate α of the entire system of *N* particles, the energy U_α will therefore be

$$U_\alpha = \frac{h^2}{8mL^2}(j_1^2+k_1^2+l_1^2+\cdots+j_N^2+k_N^2+l_N^2) \tag{8}$$

Assuming that the gas is in equilibrium with a thermal reservoir at temperature *T*, all we have to do now to determine the thermodynamic properties of the gas is to calculate *Q*, the canonical partition function, according to

$$Q = \frac{1}{N!}\sum_\alpha e^{-\beta U_\alpha} \tag{9}$$

As before, the reason for including a factor of $N!$ in Eq. (9) is to account for the indistinguishability of the gas particles.

But how are we to interpret the "sum over states" $\sum_\alpha$? Since a microstate is a specification of $3N$ quantum numbers, different microstates are just different combinations of these quantum numbers, and all of these combinations will be realized if we write

$$Q = \frac{1}{N!}\sum_\alpha e^{-\beta U_\alpha} = \frac{1}{N!}\sum_{j_1=1}^{\infty}\sum_{k_1=1}^{\infty}\sum_{l_1=0}^{\infty}\cdots\sum_{j_N=1}^{\infty}\sum_{k_N=1}^{\infty}\sum_{l_N=1}^{\infty} e^{-\beta h^2\left(j_1^2+k_1^2+l_1^2+\cdots+j_N^2+k_N^2+l_N^2\right)/(8mL^2)} \tag{10}$$

Furthermore, since we've assumed that all the particles are independent of each other, the sums in Eq. (10) all factorize. That is,

$$Q = \frac{1}{N!}\sum_{j_1=1}^{\infty} e^{-\beta h^2 j_1^2/(8mL^2)}\sum_{m_1=1}^{\infty} e^{-\beta h^2 k_1^2/(8mL^2)}\sum_{n_1=0}^{\infty} e^{-\beta h^2 l_1^2/(8mL^2)}\times\cdots$$

$$\cdots\times\sum_{j_N=1}^{\infty} e^{-\beta h^2 j_N^2/(8mL^2)}\sum_{k_N=1}^{\infty} e^{-\beta h^2 k_N^2/(8mL^2)}\sum_{l_N=1}^{\infty} e^{-\beta h^2 l_N^2/(8mL^2)} \tag{11}$$

Each of the separate sums in Eq. (11) is the same as every other, and so

$$Q = \frac{1}{N!}\left(\sum_{j_1=1}^{\infty} e^{-\beta h^2 j_1^2/(8mL^2)}\right)^{3N} \tag{12}$$

All that remains now of the statistical mechanical part of the calculation is to perform a single summation. Unfortunately, this sum can't be done exactly, but it can be evaluated approximately without significant loss of precision when the system is of macroscopic dimensions. The approximation is to replace the sum by an integral:

$$Q = \frac{1}{N!}\left(\int_0^{\infty} dj_1 e^{-\beta h^2 j_1^2/(8mL^2)}\right)^{3N} \tag{13}$$

Why this is a good approximation is because the successive terms in the summation in Eq. (12) differ so little from each other that the terms vary essentially continuously, and so for all practical purposes the sum is an integral. To see that the argument of the exponential in this equation hardly changes in going from j_1 to j_1+1, consider the case of an atom at room temperature with a mass m of 10^{-22} g in a box of side $L = 10$ cm. For this system

$$\frac{\beta h^2 (j_1+1)^2}{8mL^2} - \frac{\beta h^2 j_1{}^2}{8mL^2} = \frac{\beta h^2 (2j_1+1)}{8mL^2} \approx (2j_1+1)\times 10^{-20} \equiv \Delta$$

We've also seen that under standard temperature and pressure conditions, the quantum number j_1 is on the order of 10^9, so Δ is indeed extremely small, and no appreciable error results from replacing the sum by an integral.

The integral in Eq. (13) is well known $\left[\int_0^\infty dx e^{-ax^2} = \sqrt{\pi/a}/2\right]$, and after evaluating it, we're left with this result

$$Q = \frac{1}{N!}\left(\frac{2\pi m k_B T}{h^2}\right)^{3N/2} V^N \tag{14}$$

The Helmholtz potential of the gas is therefore given by

$$F = -k_B T\left[-\ln N! + \frac{3N}{2}\ln\left(\frac{2\pi m k_B T}{h^2}\right) + N\ln V\right]. \tag{15}$$

From the differential relation $dF = -SdT - PdV + \mu dN$, we can get the pressure as

$$P = -\left(\frac{\partial F}{\partial V}\right)_{T,N} \tag{16}$$

Differentiating Eq. (15) with respect to V at constant T and N, we see that $(\partial F/\partial V)_{T,N} = -Nk_B T/V$, and so

$$PV = Nk_B T \tag{17}$$

which is, of course, the ideal gas law.

It has obviously been much easier to derive this law within the canonical formalism than it was within the microcanonical formalism.